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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,565	05/02/2002	Audrey Goddard	P3230R1C001-168	2399

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EXAMINER	
HUNNICUTT, RACHEL KAPUST	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,565	EATON ET AL.	
	Examiner	Art Unit	
	Rachel K. Hunnicutt	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0804*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

Applicant's amendment filed August 18, 2004 is acknowledged. Claims 1-4 have been canceled. Claims 5-10 and 12 are amended. Claims 5-13 are pending and under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The objection to the specification regarding the use of trademarks is withdrawn in response to Applicant's amendments to the specification.

The rejection of claims 5-6 and 10 under 35 U.S.C. 112, second paragraph, regarding the limitation "extracellular domain...lacking its associated signal peptide" is withdrawn in response to Applicants' amendments to the claims. The rejection of claims 1-4 is withdrawn in response to Applicants' cancellation of these claims.

The rejection of claims 1-4 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,573,095 is withdrawn in response to Applicants' cancellation of these claims.

The rejection of claims 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,573,095 is withdrawn in response to Applicants' amendments to the claims. The '095 patent neither teaches nor suggests polypeptides at least 99% identical to SEQ ID NO: 58.

Claim Rejections - 35 USC § 101

The rejection of claims 1-4 under 35 U.S.C. 101 is withdrawn in response to Applicants' cancellation of these claims. The rejection of claims 5-13 under 35 U.S.C. 101 is maintained for reasons of record on p. 3-4 of the office action of paper no. 0504.

Applicants argue that the nucleic acid molecules encoding the claimed polypeptides are useful diagnostically for the determination of the presence or absence of tumor in a subject suspected of possessing a tumor as well as therapeutically as a target for the treatment of a tumor

in a subject possessing such a tumor (p. 9 of response). Applicants refer to Example 18 which shows that the mRNA for PRO1106 was more highly expressed in esophageal tumor versus normal esophagus tissue. The Exhibit A declaration of J. Christopher Grimaldi teaches that the DNA libraries used in the gene expression studies were made from pooled samples of normal and of tumor tissues. Grimaldi states in section 6 that "I conducted a semi-quantitative analysis of the expression of the DNA sequences of interest in normal versus tumor tissues. Expression levels were graded according to a scale of +, -, and +/- to indicate the amount of the specific signal detected. Using the widely accepted technique of PCR, it was determined whether the polynucleotides tested were more highly expressed, less expressed, or whether expression remained the same in tumor tissue as compared to its normal counterpart. Because this technique relies on the visual detection of ethidium bromide staining of PCR products on agarose gels, it is reasonable to assume that any detectable differences seen between two samples will represent at least a two fold difference in cDNA."

Furthermore, in Exhibit B, another declaration of J. Christopher Grimaldi, Grimaldi states that when a gene is overexpressed, the gene product or polypeptide will also be overexpressed (p. 10 of response). The declaration of Dr. Paul Polakis avers that mRNA levels typically correlate with an increase in abundance of the encoded protein (p. 10 of response). Applicants further cite Orntoft *et al.*, Hyman *et al.*, and Pollack *et al.* in support of the argument that in the vast majority of cases, the combined teachings of the art teach that gene amplification influences gene expression and that gene expression influences protein levels. In addition, Applicants refer to the declaration of Dr. Ashkenazi and cited references Hanna and Mornin who teach that even if higher levels of mRNA do not correlate with an increase in abundance of the encoded protein, that type of information is also useful in diagnosing and treating patients.

Applicant's arguments have been fully considered but have not been found to be persuasive. There is no utility for the claimed nucleic acid molecules. A utility of being a diagnostic target for esophageal tumor is a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use. This is not a substantial utility. In Example 18, the specification merely states that the gene is "more highly expressed" in one tissue as compared to another. There is no guidance in the specification as to how high the levels are. The declaration of Grimaldi (Exhibit A) does not teach the level of reproducibility

or the level of reliability of the results. Neither the specification nor the declarations provide any evidence that indicates what the differences were or whether the results were statistically significant. Applicants have provided no indication of the nature or number of samples that were used. The only thing Applicants teach is that the gene was "more highly expressed", and this does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any diseases.

Whether or not increased levels of PRO1106 mRNA correlate with increased levels of PRO1106 protein is not an issue. The declarations and cited references do not establish a substantial utility for the claimed polynucleotides, because even if increased levels of PRO1106 mRNA correlated with increased levels of the PRO1106 protein, the skilled artisan would still not be able to diagnose or treat any disease. As stated above, the specification does not provide sufficient guidance to the skilled artisan to diagnose or treat any disease.

Claim Rejections - 35 USC § 112

The rejection of claims 1-4 under 35 U.S.C. 112, first paragraph, for lack of enablement due to the invention not being supported by a specific or substantial asserted utility or a well-established utility, is withdrawn in response to the cancellation of these claims. The rejection of claims 5-13 is maintained for reasons of record on p. 4 of paper no. 0504.

The rejection of claims 1-4 under 35 U.S.C. 112, first paragraph, for lack of enablement, is withdrawn in response to Applicants' cancellation of these claims. The rejection of claims 5 and 12-13 is maintained for reasons of record on p. 5-6 of paper no. 0504. The specification does not provide enablement for polypeptides at least 99% identical to SEQ ID NO: 58 with the only limitation being that the nucleic acid encoding the polypeptide is more highly expressed in esophageal tumor than in normal esophagus tissue.

Applicants argue that the claims have been amended to include a functional recitation "wherein the nucleic acid encoding the polypeptide is more highly expressed in esophageal tumors" (p. 14 of response). Applicants further argue that "based on the detailed description of the cloning and expression of variants of SEQ ID NO: 58 in the specification, the description of

the gene expression assay, the actual reduction to practice of SEQ ID NO: 58, and the functional recitation in the instant claims", the specification enables one skilled in the art to make the invention commensurate in scope with the claims.

Applicants' arguments have been considered but have not been found to be persuasive. In this case, there is no nexus between the polypeptide's structure and the "functional" limitation. The claims require the nucleic acid encoding the polypeptide to be more highly expressed in tumor cells. How could one of skill in the art engineer such a nucleic acid molecule? The "function" is not something that the polypeptide performs. Rather, the "function" depends on the pathology of a disease. The nucleic acid molecule encoding SEQ ID NO: 58 may be upregulated in esophageal tumors, however it would be impossible to engineer a nucleic acid molecule that differs at all from one encoding SEQ ID NO: 58 that would also be upregulated in esophageal tumors. The skilled artisan would not know which sequences meet the functional and structural limitations of the claims without performing a large quantity of experimentation. The skilled artisan would need to first generate the large number of variants recited in the claims and then check to see if they are overexpressed in esophageal tumor. Undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

The rejection of claims 1-4 under 35 U.S.C. 112, first paragraph, for not complying with the written description requirement, is withdrawn in response to Applicants' cancellation of these claims. The rejection of claims 5 and 12-13 is maintained for reasons of record on p. 6-7 of paper no. 0504.

Applicants argue that the claims are not drawn to a genus of polypeptides defined only by sequence identity. Instead, based on the "detailed description of cloning and expression of variants of SEQ ID NO: 58 in the specification, the description of the gene expression assay, the actual reduction to practice of SEQ ID NO: 58 and the functional recitation in the instant claims...the claimed polypeptides are adequately described" (p. 15-16 of the response).

Applicants' arguments have been fully considered but have not been found to be persuasive. As stated above, there is no connection between the "functional" limitation and the structure of the claimed polypeptides. Nucleic acid sequences encoding polypeptides at least 99% identical to SEQ ID NO: 58 do not necessarily fall within the scope of the claimed

invention, and the specification does not provide adequate written description of the claimed genus to distinguish those sequences which are highly identical to the claimed sequences and are overexpressed in esophageal tumor versus those that are highly identical to the claimed sequences and not overexpressed in esophageal tumor. Applicants have only taught that SEQ ID NO: 57, the nucleic acid sequence encoding SEQ ID NO: 58, is overexpressed in esophageal tumor and have not provided sufficient distinguishing identifying characteristics of the genus.

Conclusion

NO CLAIMS ARE ALLOWED.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH
10/18/04

JANET ANDRES
PRIMARY EXAMINER